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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,478	10/30/2003	Richard J. Pittaro	10020502-1	2712

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EXAMINER

KAPUSHOC, STEPHEN THOMAS

ART UNIT PAPER NUMBER

1634

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/699,478	<b>Applicant(s)</b> PITTARO ET AL.	
	<b>Examiner</b> Stephen Kapushoc	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1 - 14 is/are pending in the application.
- 4a) Of the above claim(s) 1 - 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13 and 14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10-30-2003.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-12, drawn to a nanopore structure, classified in class 435, subclass 286.2.
  - II. Claims 13 and 14, drawn to a method for sensing a portion of a nanoscale moiety, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process can be performed manually, or by using alternate apparatuses such as a cleavage reaction of nucleic acid monomers for mass spectroscopic detection
3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as demonstrated by their different classification and recognized divergent subject matter and because inventions I and II require different searches that are not coextensive, examination of these claims would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Timothy Joyce on Oct. 13, 2005 a provisional election was made with traverse to prosecute the invention of Group II, claims 13 and 14. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

### ***Specification***

6. The abstract of the disclosure is objected to because the abstract is divided into two paragraphs. The MPEP describes the abstract: "the abstract should be in narrative form and generally limited to a single paragraph within the range of 50 to 150 words". Correction is required. See MPEP § 608.01(b).

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: there is no basis in the specification for the recitation of the

phrase "to quench the quencher molecule". The specification discusses only the quenching of an excited 'excitable marker' by a quencher, and makes no indication of how the quencher is itself quenched, or how this may accomplish the sensing of a nanoscale moiety.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 14 recites the limitation "to quench the quencher molecule" in part (c). The term 'quench', in reference to the use and detection of fluorescence, is used to mean a reduction in the amount of fluorescence. However, neither the claims nor the specification indicate that the quencher is excited (or in any way fluorescing), or that fluorescence is detected from the quencher. It is therefore unclear what is meant by 'quench the quencher', how this step would be accomplished, or how such a step would help to detect a nanoscale moiety.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14 includes the step (within part (c)) of moving a quencher molecule past an excitable molecule (excited in step (b)) in order 'to quench the quencher molecule'. However the specification provides no direction on how the step requiring one to 'quench the quencher' is practiced.

Prior art in the field of using fluorescence to detect particular molecular entities teaches the use of quenching agents that accept energy from excited donor molecules. The prior art uses the term 'quencher' to indicate the acceptor of energy, and the term 'quench' to indicate the acceptance of energy from an excited molecule such as a fluorophore. For example, Crockett et al (2001) describe the interaction between fluorescein and deoxyguanosine nucleotides. In this case, quenching is the decrease in the fluorescence of fluorescein due to the hybridization and close association of G residues (Fig 1). The reference teaches that the G residues are the quenchers, and the fluorescein is quenched. Similarly, Marras et al (2002) describes the interaction of several fluorophore-quencher combinations. In each case, the 'quencher' is the entity that accepts energy from the fluorophore, and 'quenching' is the measurement of the difference between the expected and observed emission from the fluorophore in the presence of the 'quencher' (Table 3). And although Marras et al teaches that a quencher may itself be a fluorophore (for example TET and TMR, p.3, right column, last

full paragraph), in its action as a quencher, the quencher is causing a change in the emission of another molecule. In no case does the prior art teach the quenching of a quencher. Furthermore, in an analysis of the quenching efficiencies of nucleotides on a variety of fluorophores, Marras et al teaches the unpredictability of the effect of any given nucleotide on any particular fluorophore. In most cases different nucleotides quench a given fluorophore to different degrees, and in some cases nucleotides enhance the detected fluorescence from the fluorophore (such as with Cy3 and any of the four nucleotides tested).

The specification provides a definition of quenching (p.13 l.17), indicating that it is a process that reduces fluorescence quantum yield without changing the fluorescence emission spectrum. The specification teaches the quenching of an excitable molecule by moving a quencher (contained on a polymer) in proximity to the excited excitable molecule (for example p.17 l.24); and teaches detection in changes of fluorescence of the excitable molecule (p.18 l.2). The specification does not teach the quenching of the quencher molecule, or the use of such a quenching event to determine the identity of the portion of a nanoscale moiety. Furthermore, while the specification mentions several molecules as being both quenchers and fluorophores (e.g. fluorescein is mentioned as a quencher (p.4 l.5) and a fluorophore (p.15 l.4)), the specification provides no working example of how any entity being used as a quencher is itself quenched, or the detection of the quenching of a quencher. The specification describes only that the fluorescence of the excitable molecule may be affected by the presence of one or more quencher molecules (p.17 l.16). Given that lack of guidance within the



specification, and the lack of direction in the prior art, it is unpredictable how one may quench a quencher molecule, and how this would lead to the detection of the nanoscale moiety.

Therefore, based on the prior art, including the level of skill and unpredictability in the art, as well as the direction provide by the specification and the lack of a working example, it is concluded that practice of the claimed invention would require an undue amount of experimentation.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/18247.

15. Claim 13 is drawn to a method for sensing a nanoscale moiety in which an excitable molecule adjacent to a nanopore is quenched in a specific manner by a portion of the nanoscale moiety, thus allowing the identification of that portion of the moiety. WO 01/18247 teaches methods for analyzing polymer molecules by detecting their effects on an optical agent. Relevant to part (a) of claim 13, WO 01/18247 specifically describes the use of a nanopore structure (p.39, Example 4 – synthetic pore) associated with an optical agent. WO 01/18247 also specifically states that the

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optical agent could be attached on either side of the pore (p.40 I.6), or on the molecular scaffold that contains the pore (p.23). WO 01/18247 provides a table of fluorophores (p. 42, Appendix A) that can be used as optical agents and includes absorbance and emission information; such fluorophores meet the definition of 'excitable marker' (p.8 I.30) as provided by the instant specification that includes 'any molecules capable of absorbing and/or releasing energy' (p.9 I.7). Relevant to part (b) of claim 13, WO 01/18247 also indicates that a polymer can be moved through the pore (p.40 I.6), with (in the case of a nucleic acid polymer) base-specific interaction between the monomers of the polymer and the excited optical agent allowing for identification of the particular monomers (p.36 – Reporter group excitation and base-specific interaction). In the method described in WO 01/18247 for the analysis of a nucleic acid polymer (which is a nanoscale moiety), the nucleic acid serves as a quencher molecule, with each base performing a distinguishable quenching action on an excited fluorophore (the fluorophore being an excitable molecule (p.35 – Excitation and detection of fluorescence; Appendix A)).

### ***Conclusion***

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-


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272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Stephen Kapushoc  
Art Unit 1634

  
JULIET C. SWITZER  
PRIMARY EXAMINER 10/27/05